UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,383	09/19/2006	Elliott P. Dawson	16304-1US	7404

23676 7590 12/02/2011

SHELDON MAK & ANDERSON PC
100 Corson Street
Third Floor
PASADENA, CA 91103-3842

EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
12/02/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,383	DAWSON ET AL.	
	Examiner	Art Unit	
	JANE ZARA	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *33-79 and 81-86* is/are pending in the application.

5a) Of the above claim(s) *33-52,54-79 and 81-86* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *53* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/GB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 10-20-10.

Claims 33-79, 81-86 are pending in the instant application.

Claims 33-52, 54-79, 81-86 have been withdrawn as non-elected inventions.

Claim 53 has been examined on its merits as set forth below.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-20-10 has been entered.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Applicant's arguments with respect to claim 53 have been considered but are moot in view of the new ground(s) of rejection as set forth below.

Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 53 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 53 depends from claim 33, which recites nuclease resistant nucleotides comprising a *phosphorothioate backbone*, but no support for this limitation has been found in the original specification and is therefore considered to be new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobsen et al (US 2005/0272075) in view of Shapero et al (US 2005/0153347) and Baracchini et al (USPN 5,801,154).

The claim is drawn to a method of isolating a microRNA of interest comprising providing a set of capture probes with a first adapter segment having a first adapter segment sequence, the first adapter segment comprising a 3' end and a 5' end, a second adapter segment having a second adapter segment sequence comprising a 3' end and a 5' end, which different capture probes each comprise different first adapter sequences from each other, and which capture probes also comprise different microRNA binding segments, each having a microRNA binding segment sequence that is substantially complementary to a different microRNA of interest, wherein the 5' end of the first adapter segment connects to the 3' end of the microRNA binding segment, the 3' end of the second adapter segment is connected to the 5' end of the microRNA binding segment, providing a first linker and a second linker, combining these components with a sample comprising one or more microRNAs of interest, allowing the first linker for each capture probe to hybridize with its corresponding first adapter segment, the microRNA of interest to hybridize with the microRNA binding segment and the second linker to hybridize with the second adapter segment, ligating the 3' end of the first linker that is hybridized to the first adapter segment to the 5' end of the microRNA of interest that is hybridized to the microRNA binding segment, and ligating

the 3' end of the microRNA of interest that is hybridized to the microRNA binding segment to the 5' end of the second linker that is hybridized to the second adapter segment, wherein a complex is produced upon ligation comprising a ligated first linker – microRNA of interest – second linker which is hybridized to each of the corresponding capture probes, and wherein the first linker is complementary to the first adapter segment of the corresponding capture probe and the second linker is complementary to a second adapter segment of the capture probe, dehybridizing the capture probe from the strand of the ligated first linker – microRNA of interest – second linker. The claimed invention is further drawn to purifying the ligated first linker – microRNA of interest – second linker that has been dehybridized from the capture probe by applying DNAase to a solution containing the ligated first linker – miroRNA of interest – second linker, which linkers have been rendered nuclease resistant by the incorporation of nuclease resistant internucleotide linkages including the incorporation of phosphorothioate backbone moieties, then circularizing the ligated first linker - microRNA of interest - second linker, then treating the circularized entity with one or more exonucleases.

Jacobsen et al (US 2005/0272075) teach methods of isolating microRNA of interest from a sample comprising microRNA of interest, the method comprising providing a capture probe, wherein the capture probe has a first adapter segment sequence, wherein the first capture probe has a microRNA binding segment sequence, which microRNA binding segment is substantially complementary to and hybridizes to one or more microRNAs of interest, and wherein the 5' end of the first adapter segment is connected to the 3' end of the microRNA binding segment, and the 3' end of the

second adapter segment is connected to the 5' end of the microRNA binding segment, providing a first linker and a second linker, combining the sample, the capture probe, first and second linkers, allowing the first linker to hybridize with the first adapter segment, the microRNA to hybridize with the microRNA binding segment, the second linker to hybridize with the second adapter segment, ligating the 3' end of the first linker (which is hybridized to the first adapter segment) to the 5' end of the microRNA of interest (which is hybridized to the microRNA binding segment), ligating the 3' end of the microRNA of interest (which is hybridized to the microRNA binding segment) to the 5' end of the second linker (which is hybridized to the second adapter segment), dehybridizing the capture probe from the ligated strand, wherein the first linker binds to a substantially complementary first adapter segment of the capture probe, and the second linker hybridizes to a substantially complementary second adapter segment of the capture probe (see entire document, esp. pp. 4-5, 9-101515-2124-25, 27, 37, 45-48).

Jacobsen does not teach a set of capture probes that target different microRNA molecules.

Shapero et al (US 2005/0153347) teach methods of enriching nucleic acid products in a solution comprising the circularization of, e.g., extended capture probes and ligating the juxtaposed ends, followed by digestion of the non-circularized fragments with exonuclease (see esp. ¶¶ 0102-0104).

Baracchini et al (USPN 5,801,154) the incorporation of phosphorothioates and other modifications into internucleotide linkages for enhancing oligonucleotides and polynucleotides from nuclease degradation (see esp. col. 6-8).

It would have been obvious to design additional capture probes relying on the those initially taught by Jacobsen, but comprising additional and distinct adapter segment sequences and comprising different microRNA binding segments for capturing multiple, different microRNAs of interest from a solution. This would involve synthesizing capture probes capable of ligations as originally described by Jacobsen, but using several distinct capture probes designed to bind to different microRNAs of interest, and designed to be captured by distinct adapter segments on the corresponding capture probes. One of skill would have been motivated to design and use multiple and distinct capture probes as instantly claimed in order to fish out multiple microRNAs of interest from the same solution, and partially isolating these different microRNAs utilizing the different adaptor sequences and different ligation products. One of skill would reasonably expect that the distinct capture probes would be used to successfully identify multiple microRNA molecules within the same solution because it would involve minor adaptations of the original capture probes taught by Jacobsen, incorporating different adaptor sequences and microRNA binding segments that are distinct from each other and easily separated in a solution. The ligation reactions generating the captured molecules comprising microRNA target molecules of interest flanked by ligated first and second linkers hybridized to corresponding capture probes

would merely involve a modification of capture probes bearing distinct adaptor and microRNA binding sequences, each with distinct adaptor segments.

, it would have been obvious to degrade unwanted by-products from the desired captured microRNA fragments by incorporating nuclease resistant moieties, including phosphorothioate internucleotide linkages into the first linker - microRNA of interest - second linker products because such nuclease resistant oligonucleotides were well known in the art at the time of the invention, as taught previously by Baracchini. One would have been motivated to use this enrichment step to enrich for the desired captured nucleic acid products to simplify their subsequent analyses by removing unwanted by-products, including the removal of unhybridized, unligated fragments, etc. It also would have been obvious to utilize well known techniques of enrichment including the well known means of circularizing captured fragments, in the instant case, via a second round of ligation of the ligated first linker - microRNA of interest - second linker, in turn circularizing these fragments then treating the circularized entities with one or more exonucleases, because such enrichment techniques were well known in the field of molecular biology at the time of the invention as taught previously by Shapero. One would have been motivated to do so to enrich for the desired captured nucleic acid products to simplify their subsequent analyses by removing unwanted by-products, including the removal of unhybridized fragments, etc. One of skill in the art would have reasonably expected that the incorporation of nuclease resistant linkages, as well as the subsequent enrichment of circularized products in the presence of exonucleases would provide for solutions with enriched products comprising first linker -

microRNA of interest - second linker products, better enabling their subsequent analyses.

For these reasons, the instant invention would have been obvious to one of skill in the art at the time of filing.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** The examiner's office hours are generally Monday-Friday, 10:30am - 7pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita, can be reached on (571) 272-2876. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
12-1-11

/Jane Zara/

Primary Examiner, Art Unit 1635